



R<sup>3</sup> and R<sup>4</sup> are independently selected from hydrogen, (1-6C)alkyl, (3-8C)cycloalkyl, (3-8C)cycloalkenyl, (5-12C)bicycloalkyl, -(1-6C)alkyl(3-8C)cycloalkyl, -(1-6C)alkyl(3-8C)cycloalkenyl, AR1, AR2, HET1, HET2, -(1-6C)alkylAR1, -(1-6C)alkylAR2, -(1-6C)alkylHET1, and -(1-6C)alkylHET2; or

R<sup>3</sup> and R<sup>4</sup> together form a ring as defined by (3-8C)cycloalkyl, AR2, HET1 or HET2;

R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup> and R<sup>8</sup> are independently selected from hydrogen and (1-6C)alkyl; wherein any (1-6C)alkyl group within any definition of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup> or R<sup>8</sup> is optionally substituted by 1 or 2 substituents independently selected from hydroxy and fluoro; wherein any (3-8C)cycloalkyl, (3-8C)cycloalkenyl, (5-12C)bicycloalkyl or (6-12C)tricycloalkyl within any definition of R<sup>2</sup>, R<sup>3</sup> or R<sup>4</sup> is optionally substituted;

AR1 is optionally substituted phenyl;

AR2 is an optionally substituted 8-, 9- or 10-membered, unsaturated, partially or fully saturated bicyclic carbocyclic ring;

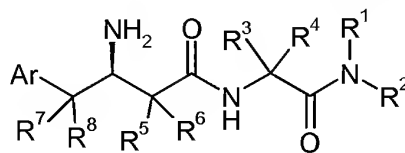
HET1 is an optionally substituted 3-, 4-, 5- or 6-membered, unsaturated, partially or fully saturated monocyclic heterocyclyl ring containing up to four heteroatoms independently selected from O, N and S<sub>x</sub> [[[ ]]] but not containing any O-O, O-S or S-S bonds[[ ]]], linked via a ring carbon atom, or a ring nitrogen atom if the ring is not thereby quaternised, and wherein any available carbon, sulfur or nitrogen atom may be oxidised;

HET2 is an optionally substituted 8-, 9- or 10-membered, unsaturated, partially or fully saturated bicyclic heterocyclyl ring containing up to four heteroatoms independently selected from O, N and S<sub>x</sub> [[[ ]]] but not containing any O-O, O-S or S-S bonds[[ ]]], and linked via a ring carbon atom in either of the rings comprising the bicyclic system;

HET3 is an N-linked saturated bicyclic or tricyclic ring system, containing up to 12 ring atoms including the linking nitrogen atom;

wherein suitable optional substituents on (3-8C)cycloalkyl, (5-12C)bicycloalkyl, (6-12C)tricycloalkyl, AR1, AR2, HET1 and HET2 are 1, 2, 3, 4 or 5 substituents independently selected from phenyl [[[ ]]] optionally substituted with halo, trifluoromethyl, (1-4C)alkyl or (1-4C)alkoxy[[ ]]], halo, (1-6C)alkyl, halo(1-6C)alkyl, dihalo(1-6C)alkyl, trifluoromethyl, (1-6C)alkoxy, carboxy(1-6C)alkyl, carboxy(1-6C)alkoxy, hydroxy, amino, (1-6C)alkylamino, di(1-6C)alkylamino, -CONH<sub>2</sub>, -CONH(1-6C)alkyl, -CONdi(1-6C)alkyl, -NHCO(1-6C)alkyl, -SO<sub>2</sub>(1-6C)alkyl, -S(O)<sub>2</sub>NH<sub>2</sub>, -SO<sub>2</sub>NH(1-6C)alkyl, -SO<sub>2</sub>Ndi(1-6C)alkyl and -NHSO<sub>2</sub>(1-6C)alkyl.

2. (original) A compound as claimed in Claim 1 which is a compound of the formula (IA)



(IA)

or a pharmaceutically acceptable salt thereof, wherein Ar, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup> and R<sup>8</sup> have any of the meanings defined in Claim 1.

3. (currently amended) A compound as claimed in Claim 1-~~or~~2 or a pharmaceutically-acceptable salt thereof, wherein:

Ar is phenyl optionally substituted with 1, 2, 3, 4 or 5 groups independently selected from R<sup>9</sup>;

R<sup>9</sup> is selected from halo, (1-6C)alkyl [([ ]optionally substituted with 1-5 halo[ ])], (1-6C)alkoxy [([ ]optionally substituted with 1-5 halo[ ])], and cyano;

R<sup>1</sup> is selected from hydrogen and (1-6C)alkyl;

R<sup>2</sup> is selected from hydrogen, (1-6C)alkyl, (3-8C)cycloalkyl, (5-12C)bicycloalkyl, (6-12C)tricycloalkyl, AR1, HET1, -(1-6C)alkylAR1, -(1-6C)alkylAR2, -(1-6C)alkyl(3-8C)cycloalkyl, -(1-6C)alkylHET1, -(1-6C)alkylHET2, -(1-6C)alkylCO<sub>2</sub>(1-6C)alkyl, -(1-6C)alkylCO<sub>2</sub>(3-8C)cycloalkyl, -(1-6C)alkylCO<sub>2</sub>AR1, -(1-6C)alkylCO<sub>2</sub>HET1, -(1-6C)alkylOCO(1-6C)alkyl, -(1-6C)alkylOCO(3-8C)cycloalkyl, -(1-6C)alkylOCOAR1, -(1-6C)alkylOCOHET1, -(1-6C)alkylCO(1-6C)alkyl, -(1-6C)alkylCO(3-8C)cycloalkyl, -(1-6C)alkylCOAR1, -(1-6C)alkylCOHET1, -(1-6C)alkylINHCO(1-6C)alkyl, -(1-6C)alkylINHCO(3-8C)cycloalkyl, -(1-6C)alkylINHCOAR1, -(1-6C)alkylCONH(1-6C)alkyl, -(1-6C)alkylCONH(3-8C)cycloalkyl, -(1-6C)alkylCON-di(1-6C)alkyl, -(1-6C)alkylCONHAR1, -(1-6C)alkylNH(1-6C)alkyl, -(1-6C)alkylN-di(1-6C)alkyl, -(1-6C)alkylINHAR1, -(1-6C)alkylNH(HET1), -(1-6C)alkylNH<sub>2</sub>SO<sub>2</sub>(1-6C)alkyl, -(1-6C)alkylSO<sub>2</sub>NH(1-6C)alkyl, and -(1-6C)alkylSO<sub>2</sub>N-di(1-6C)alkyl; or

R<sup>1</sup> and R<sup>2</sup> may together with the nitrogen to which they are attached form a ring defined by HET1; wherein a ring comprising R<sup>1</sup> and R<sup>2</sup> is optionally substituted by 1 or 2 substituents independently selected from halo, (1-6C)alkyl, halo(1-6C)alkyl, (1-6C)alkoxy, cyano, carboxy, carboxy(1-6C)alkyl, -CO(1-6C)alkyl, -CO<sub>2</sub>(1-6C)alkyl, (1-6C)alkylamino, di-(1-6C)alkylamino, -NHCO(1-6C)alkyl, -CONH(1-6C)alkyl, -CONdi-(1-6C)alkyl and HET1;

R<sup>3</sup> and R<sup>4</sup> are independently selected from hydrogen, (1-6C)alkyl, -(1-6C)alkyl(3-8C)cycloalkyl, -(1-6C)alkyl(3-8C)cycloalkenyl, -(1-6C)alkylAR1, -(1-6C)alkylAR2, -(1-6C)alkylHET1, and -(1-6C)alkylHET2; or

R<sup>3</sup> and R<sup>4</sup> together form a ring as defined by (3-8C)cycloalkyl, AR2, HET1 or HET2;

R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup> and R<sup>8</sup> are independently selected from hydrogen and (1-6C)alkyl;

AR1 is optionally substituted phenyl;

AR2 is an optionally substituted 8-, 9- or 10-membered, unsaturated, partially or fully saturated bicyclic carbocyclic ring;

HET1 is an optionally substituted 3-, 4-, 5- or 6-membered, unsaturated, partially or fully saturated monocyclic heterocyclyl ring containing up to four heteroatoms independently selected from O, N and S<sub>x</sub> [[[ ]]] but not containing any O-O, O-S or S-S bonds[[ ]]], linked via a ring carbon atom, or a ring nitrogen atom if the ring is not thereby quaternised, and wherein any available carbon, sulfur or nitrogen atom may be oxidised;

HET2 is an optionally substituted 8-, 9- or 10-membered, unsaturated, partially or fully saturated bicyclic heterocyclyl ring containing up to four heteroatoms independently selected from O, N and S<sub>x</sub> [[[ ]]] but not containing any O-O, O-S or S-S bonds[[ ]]], and linked via a ring carbon atom in either of the rings comprising the bicyclic system;

wherein suitable optional substituents on AR1, AR2, HET1 and HET2 are 1, 2, 3, 4 or 5 substituents independently selected from halo, (1-6C)alkyl, halo(1-6C)alkyl, dihalo(1-6C)alkyl, trifluoromethyl, (1-6C)alkoxy, carboxy(1-6C)alkyl, carboxy(1-6C)alkoxy, hydroxy, amino, (1-6C)alkylamino, di(1-6C)alkylamino, -CONH<sub>2</sub>, -CONH(1-6C)alkyl, -CONdi(1-6C)alkyl, -NHCO(1-6C)alkyl, -S(O)<sub>2</sub>NH<sub>2</sub>, -SO<sub>2</sub>NH(1-6C)alkyl, -SO<sub>2</sub>Ndi(1-6C)alkyl and -NHSO<sub>2</sub>(1-6C)alkyl.

4. (currently amended) A compound of the formula (I) as claimed in Claim 1 claim-1 or-2 or a pharmaceutically acceptable salt thereof wherein

Ar is phenyl optionally substituted with 1 or 2 groups independently selected from R<sup>9</sup>;

R<sup>9</sup> is selected from halo, methyl, methoxy and trifluoromethyl;

R<sup>1</sup> is hydrogen or methyl;

R<sup>5</sup> is hydrogen;

R<sup>6</sup> is hydrogen;

R<sup>7</sup> is hydrogen;

R<sup>8</sup> is hydrogen;

R<sup>3</sup> and R<sup>4</sup> together form a ring as defined by AR2, HET1 or HET2; and

R<sup>2</sup> is selected from (1-6C)alkyl, (3-8C)cycloalkyl, (5-12C)bicycloalkyl, (6-12C)tricycloalkyl, AR1, HET1, -(1-6C)alkylAR1, -(1-6C)alkylNHCO(1-6C)alkyl,

-(1-6C)alkylNHCOAR1, -(1-6C)alkylCONH(1-6C)alkyl, -(1-6C)alkylCONHAR1,  
 -(1-6C)alkylNH(1-6C)alkyl, -(1-6C)alkylINHAR1, -(1-6C)alkylNH(HET1),  
 -(1-6C)alkylNH<sub>2</sub>SO<sub>2</sub>(1-6C)alkyl and -(1-6C)alkylSO<sub>2</sub>NH(1-6C)alkyl.

5. (currently amended) A compound of the formula (I) as claimed in Claim 1 or 2 or a pharmaceutically acceptable salt thereof wherein

Ar is phenyl optionally substituted with 1 or 2 groups independently selected from R<sup>9</sup>;

R<sup>9</sup> is selected from halo, methyl, methoxy and trifluoromethyl;

R<sup>1</sup> is hydrogen or methyl;

R<sup>5</sup> is hydrogen;

R<sup>6</sup> is hydrogen;

R<sup>7</sup> is hydrogen;

R<sup>8</sup> is hydrogen;

R<sup>3</sup> is hydrogen and R<sup>4</sup> is selected from -(1-4C)alkyl(3-8C)cycloalkyl,

-(1-4C)alkyl(3-8C)cycloalkenyl, -(1-4C)alkylAR1, -(1-4C)alkylAR2, -(1-4C)alkylHET1 and  
 -(1-4C)alkylHET2; and

R<sup>2</sup> is selected from (1-6C)alkyl, (3-8C)cycloalkyl, (5-12C)bicycloalkyl,  
 (6-12C)tricycloalkyl, AR1, HET1, -(1-6C)alkylAR1, -(1-6C)alkylNHCO(1-6C)alkyl,  
 -(1-6C)alkylNHCOAR1, -(1-6C)alkylCONH(1-6C)alkyl, -(1-6C)alkylCONHAR1,  
 -(1-6C)alkylNH(1-6C)alkyl, -(1-6C)alkylINHAR1, -(1-6C)alkylNH(HET1),  
 -(1-6C)alkylNH<sub>2</sub>SO<sub>2</sub>(1-6C)alkyl and -(1-6C)alkylSO<sub>2</sub>NH(1-6C)alkyl.

6. (currently amended) A compound as claimed in Claim 1 ~~claim 1 or 2~~ or a pharmaceutically acceptable salt thereof wherein

Ar is phenyl substituted with 1, 2 or 3 fluoro;

R<sup>1</sup> is hydrogen;

R<sup>2</sup> is selected from (1-6C)alkyl, (3-8C)cycloalkyl, (5-12C)bicycloalkyl,  
 (6-12C)tricycloalkyl, AR1, HET1, -(1-6C)alkylAR1, -(1-6C)alkylNHCO(1-6C)alkyl,  
 -(1-6C)alkylNHCOAR1, -(1-6C)alkylCONH(1-6C)alkyl, -(1-6C)alkylCONHAR1,  
 -(1-6C)alkylNH(1-6C)alkyl, -(1-6C)alkylINHAR1 and -(1-6C)alkylNH(HET1),  
 -(1-6C)alkylNH<sub>2</sub>SO<sub>2</sub>(1-6C)alkyl and -(1-6C)alkylSO<sub>2</sub>NH(1-6C)alkyl; [.]

R<sup>3</sup> is hydrogen;

R<sup>4</sup> is CH<sub>2</sub>-AR1, CH<sub>2</sub>-HET1 or CH<sub>2</sub>-HET2; and

R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup> and R<sup>8</sup> are all hydrogen.

7. (currently amended) A compound as claimed in Claim 1 or 2 or a pharmaceutically acceptable salt thereof wherein

Ar is phenyl substituted with 1, 2 or 3 fluoro;

R<sup>1</sup> is hydrogen;

R<sup>2</sup> is hydrogen, (1-4C)alkyl, -(1-4C)alkylAR<sup>1</sup> or -(1-4C)alkylCONH(1-4C)alkyl;

R<sup>3</sup> is hydrogen;

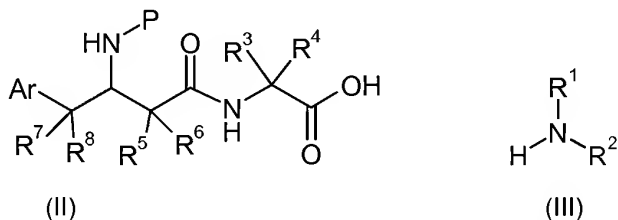
R<sup>4</sup> is CH<sub>2</sub>-AR<sup>1</sup> or CH<sub>2</sub>-HET<sup>1</sup>; and

R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup> and R<sup>8</sup> are all hydrogen.

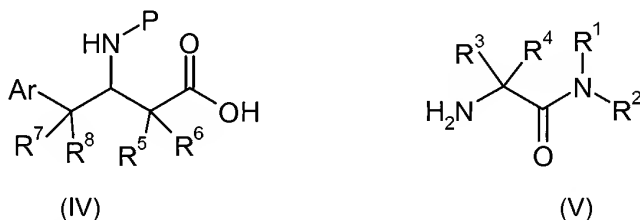
8. (currently amended) A compound as claimed in Claim 5 ~~claim 5, 6 or 7~~ or a pharmaceutically acceptable salt thereof, wherein the carbon atom bearing R<sup>3</sup> and R<sup>4</sup> has the (R)-configuration.

9. (currently amended) A compound as claimed in Claim 1 ~~claim 1~~ which is selected from  
 (R)-3-Amino-*N*-((R)-1-benzylcarbamoyl-2-phenyl-ethyl)-4-(2-fluoro-phenyl)-butyramide;  
 (R)-3-Amino-4-(2-fluoro-phenyl)-*N*-((R)-1-methylcarbamoyl-2-phenyl-ethyl)-butyramide;  
 (R)-3-Amino-4-(2-fluoro-phenyl)-*N*-[(R)-1-(methylcarbamoylmethyl-carbamoyl)-2-phenyl-ethyl]-butyramide;  
 (R)-3-Amino-4-(2-fluoro-phenyl)-*N*-((R)-1-methylcarbamoyl-2-thiophen-2-yl-ethyl)-butyramide;  
 (R)-3-Amino-4-(2-fluoro-phenyl)-*N*-[(R)-2-(1*H*-indol-3-yl)-1-methylcarbamoyl-ethyl]-butyramide;  
 (R)-3-Amino-*N*-[(R)-2-(4-chloro-phenyl)-1-methylcarbamoyl-ethyl]-4-(2-fluoro-phenyl)-butyramide;  
 (R)-3-Amino-*N*-[(R)-2-(4-methyl-phenyl)-1-methylcarbamoyl-ethyl]-4-(2-fluoro-phenyl)-butyramide;  
 (R)-3-Amino-4-(2-fluoro-phenyl)-*N*-((R)-1-methylcarbamoyl-2-pyridin-3-yl-ethyl)-butyramide;  
 (R)-3-Amino-4-(2-fluoro-phenyl)-*N*-((R)-1-methylcarbamoyl-2-pyridin-4-yl-ethyl)-butyramide;  
 (R)-3-Amino-*N*-[(R)-2-(4-bromo-phenyl)-1-methylcarbamoyl-ethyl]-4-(2-fluoro-phenyl)-butyramide;  
 (R)-3-Amino-4-(2-fluoro-phenyl)-*N*-((R)-1-methylcarbamoyl-2-thiophen-3-yl-ethyl)-butyramide;  
 (R)-3-Amino-4-(2-fluoro-phenyl)-*N*-((R)-1-methylcarbamoyl-2-pyridin-2-yl-ethyl)-butyramide;  
 and  
 (R)-3-Amino-*N*-(1-carbamoyl-2-furan-2-yl-ethyl)-4-(2-fluoro-phenyl)-butyramide; or a pharmaceutically-acceptable salt thereof.

10. (currently amended) A process for the preparation of a compound of formula (I), or a pharmaceutically acceptable salt thereof, as claimed in Claim 1 ~~claim 1~~ which comprises  
 a) coupling of a compound of formula (II) or an activated derivative thereof, wherein P is an amino protecting group, with a compound of formula (III), followed by removal of the protecting group P;



or b) coupling of a compound of formula (IV) or an activated derivative thereof, wherein P is an amino protecting group, with a compound of formula (V) followed by removal of the protecting group P;



and thereafter if desirable or necessary

- (i) converting a compound of formula (I) into another compound of formula (I) using conventional functional group modification; and/or
- (ii) optionally forming a pharmaceutically acceptable salt; and wherein Ar, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup> and R<sup>8</sup> have any of the meanings defined in Claim 1.

11. (currently amended) A pharmaceutical composition which comprises a compound of formula (I) or (IA) as claimed in ~~any one of claims 1 to 9~~ Claim 1 or a pharmaceutically-acceptable salt thereof, in association with a pharmaceutically-acceptable excipient or carrier.

12-13. (cancelled)

14. (new) A compound as claimed in Claim 6 or a pharmaceutically acceptable salt thereof, wherein the carbon atom bearing R<sup>3</sup> and R<sup>4</sup> has the (R)-configuration.

15. (new) A compound as claimed in Claim 7 or a pharmaceutically acceptable salt thereof, wherein the carbon atom bearing R<sup>3</sup> and R<sup>4</sup> has the (R)-configuration.

16. (new) A method for producing an inhibition of DPP-IV activity in a warm-blooded animal, such as a human being, in need of such treatment which comprises administering to said animal an effective amount of a compound of formula (I), as claimed in Claim 1, or a pharmaceutically-acceptable salt thereof as defined hereinbefore.

17. (new) A method of treating diabetes mellitus in a warm-blooded animal, such as a human being, in need of such treatment which comprises administering to said animal an effective amount of a compound of formula (I) or a pharmaceutically-acceptable salt thereof as claimed in Claim 1.